

Appeal Brief  
Serial No. 09/869,630  
Attorney Docket No. PZ9847 US

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of : Knox et al.  
Application No. : 09/869,630  
Filing Date : September 21, 2001  
Art Unit : 1641  
Title : NMR Spectroscopy Method  
Docket No. : PZ9847 US

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**APPEAL BRIEF**

## TABLE OF CONTENTS

	<u>Page</u>
I. Real Party In Interest .....	1
II. Related Appeals and Interferences.....	1
III. Status of Claims .....	1
IV. Status of Amendments .....	1
V. Summary of Claimed Subject Matter .....	1
VI. Grounds Of Rejection To Be Reviewed On Appeal.....	2
VII. Argument .....	3
A. The Examiner's Rejections of the Claims Should be Reversed Since Rose and Pines, Individually or In Combination, Fail to Teach All the Elements of the Claims .....	3
XIII. Claims Appendix .....	11
IX. Evidence Appendix.....	13
X.....Related Proceedings Appendix.....	14

**I. REAL PARTY IN INTEREST**

The real party in interest in this Appeal is Amersham plc (now GE Healthcare Limited, a part of General Electric “GE”).

**II. RELATED APPEALS AND INTERFERENCES**

There are no other appeals or interferences related to the instant appeal.

**III. STATUS OF CLAIMS**

Claims 1 and 3-10 are pending in this application. The Examiner has rejected all of these claims. Claims 1 and 3-10 as amended during prosecution are reproduced in the **Claims Appendix** attached hereto. Appellants are appealing the rejections of Claims 1 and 3-10.

**IV. STATUS OF AMENDMENTS**

Appellants filed a Response on May 2, 2006 and a final office action was mailed on July 25, 2006. No claims were amended subsequent to the Examiner’s final rejection that was mailed on July 25, 2006.

**V. SUMMARY OF CLAIMED SUBJECT MATTER**

Independent Claim 1 describes an *in vitro* method which is a test involving a reaction of one or more biological molecules which comprises labeling one of said biological molecules with hyperpolarized <sup>129</sup>Xe, wherein an assay reagent comprises said biological molecule; conducting said reaction; and observing a magnetic response resonance (NMR)

spectrum and/or NMR image of the hyperpolarized  $^{129}\text{Xe}$  during the course of said reaction in order to detect a conformational change in the labeled biological molecule.

Independent Claim 10 describes an *in vitro* assay method for following the progress of a reaction of one or more biological molecules and which comprises: labeling an assay reagent with hyperpolarized  $^{129}\text{Xe}$ , wherein said assay reagent comprises one of said one or more biological molecules; conducting said reaction; and observing a change with time of a magnetic response resonance (NMR) spectrum and/or NMR image of the hyperpolarized  $^{129}\text{Xe}$  during the course of said reaction in order to detect a conformational change in the labeled assay reagent.

## **VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL**

The issues for review in this appeal arise from a Final Rejection that was mailed on July 25, 2006. The Examiner rejected claims 1 and claims 3-10 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,015,565 (“Rose”) in view of U.S. Patent No. 6,426,058 (“Pines”). Therefore, the issues in this appeal are:

1. Whether Rose in view of Pines individually or in combination, disclose, teach, or suggest all the elements of claims 1 and 3-10?

## **VII. ARGUMENT**

The Examiner rejected Claims 1 and 3-10 under 35 U.S.C. § 103 (a) as being unpatentable over U.S. Patent No. 6,015,565 (“Rose”) in view U.S. Patent No. 6,426,058 (“Pines”).

Appellants respectfully request that The Board of Patent Appeals and Interferences (“Board”) should reverse the Examiner’s rejections for the reasons set forth below.

### **A. The Examiner’s Rejections of the Claims 1 and 3 – 10 Should be Reversed Since Rose and Pines Individually or In Combination, Fail to Teach All the Elements of the Claims**

Claims 1 and 10 of the present invention are directed to an *in vitro* method which is a test involving a reaction of one or more biological molecules. The methods of claims 1 and 10 include the steps of:

labeling one of the biological molecules with hyperpolarized  $^{129}\text{Xe}$ , wherein an assay reagent includes the biological molecule;  
conducting the reaction; and  
observing the magnetic resonance (NMR) spectrum and/or NMR image of the hyperpolarized  $^{129}\text{Xe}$  during the course of said reaction in order to detect any conformational change in the labeled biological molecule.

Rose discloses combining a pharmaceutical candidate with glycoprotein B and thereafter detecting whether the pharmaceutical candidate has bound to the active site of glycoprotein B and thus inducing a functional change in glycoprotein B.

Pines teaches the use of  $^{129}\text{Xe}$  to enhance NMR detection by transfer of polarization from  $^{129}\text{Xe}$  to NMR active nuclei in a sample being analyzed.

Before disguising the specific differences between the prior art and the present invention, Appellants respectfully submit that it is impermissible within the framework of 35 U.S.C. §103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443 (Fed. Cir. 1986). (emphasis added).

Appellants contend that no motivation to combine exists because Rose itself teaches different methods for carrying out the detection step in comparison to the present invention, e.g. that binding of the candidate to the glycoprotein B may be observed as a conformational change, which may be detected using nuclear magnetic resonance (NMR). Additionally, Appellants further contend that no motivation to combine exists because Rose itself does not teach, disclose or suggest the NMR spectrum and/or image is observed during the course of the reaction between the candidate and glycoprotein B, as would be required if either of the methods of claims 1 or 10 of the present invention were being used. At this point Appellants respectfully point out that on the bottom of page 4 through page 5, line 2 of the

Office Action dated July 26, 2006 (“Office Action”) the Examiner states “Applicant argues on page 3 that Rose does not disclose that the NMR spectrum and/or image is observed during the course of the reaction as required by the present claims. This is not persuasive because the detection of the binding is a detection during the course of the reaction.” Appellants respectfully disagree. The detection step of Rose is temporally separate to the reaction itself whereas in claims 1 and 10 of the present invention, the detection step takes place at the same time as, or during the course of, the reaction.

Furthermore, on the bottom of page 2 through page 3, line 2 of the Office Action, the Examiner states that “Rose does not explicitly disclose labeling the biological molecule with hyperpolarized <sup>129</sup>Xe to enhance NMR detection. Pine et al. however discloses this limitation.” However, there is nothing in Pines that discloses, suggests, or teaches the observation of an NMR spectrum and/or image during the course of the reaction, as required by claims 1 and 10 of the present invention.

Accordingly, Appellants respectfully point out here that it is well settled in the law that a reference must be considered not just for what it expressly teaches, but also for what it fairly suggests to one who is unaware of the claimed invention. *In re Baird*, 16 F.3d 380, (Fed. Cir. 1994).

Appellants also submit that the present invention describes at length the monitoring of a reaction through magnetic resonance (NMR) spectrum in order to detect any unforeseen or variable conformational changes in a labeled biological molecule. None of these

problems were recognized in the prior art, and hence the cited references simply cannot provide a motivation to essentially apply magnetic resonance (NMR) spectrum to monitoring a reaction in order to detect any unforeseen or variable conformational changes in a labeled biological molecule. The solution to the problem provided by the present claims is believed non-obvious for this reason.

Furthermore, the invention as taught by Rose at Columns 5 through 7 has many features: e.g.

- isolating polynucleotides, polypeptides, and antibodies derived from or reactive with products encoding Glycoprotein B molecules;
- obtaining polynucleotides comprising linear sequences of amino acids;
- isolating a monoclonal antibody specific for a Glycoprotein B polypeptide;
- obtaining a vaccine comprising a polypeptide;
- inhibiting attachment of a herpes virus to a cell;
- isolating an amplified copy of a polynucleotide encoding a Glycoprotein B;
- detecting viral DNA or RNA in a sample;
- etc.

Of all of these features, Appellants find it difficult to believe that Rose would even suggest improving its invention by labeling a biological molecule with hyperpolarized <sup>129</sup>Xe to enhance NMR detection. It is well settled that a reference must be considered not just for what it expressly teaches, but also for what it fairly suggests to one who is unaware of the claimed invention. *In re Baird*, 16 F.3d 380, (Fed. Cir. 1994). The Examiner's reasoning ignores the fact that Rose gives no description, at all, about labeling a biological molecule with hyperpolarized <sup>129</sup>Xe to enhance NMR detection but expounds at length about the other features of the invention. The Examiner fails to demonstrate why one of ordinary skill in the art, upon reading Rose, would

be motivated to select labeling a biological molecule with hyperpolarized  $^{129}\text{Xe}$  to enhance NMR detection – of all things – as the key to ‘improving’ Rose. Appellants contend that the Examiner has failed to show why the person skilled in the art would select only labeling a biological molecule with hyperpolarized  $^{129}\text{Xe}$  to enhance NMR detection from this long list of features to seek to improve, and as a consequence choose not to improve all the other aspects even those which Rose teaches as important. In this respect the Appellants respectfully submit that the Examiner has failed to make a *prima facie* case of obviousness in rejecting the present invention.

Additionally, even assuming, *arguendo*, that the references are properly combinable; Appellants respectfully submit that any such combination would teach away from the present invention. ‘Teaching away’ simply means teaching a solution that would not lead to the claimed subject matter. As noted by the Federal Circuit:

A reference may be said to teach away when a person of ordinary skill, upon [examining] the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. (emphasis added).

*Para-Ordnance Mfg. v. SGS Importers Int'l*, 73 F.3d 1085 (Fed. Cir. 1995).

Appellants respectfully submit that the mere fact that a reference may suggest an ‘improvement’ does not dictate that the improvement will direct one to all other ‘improvements’. That is, one improvement can teach away from another, as the two improvements may diverge from each other in their teachings. The *Para-Ordnance* decision (above) clearly states that teaching away does not require a negative teaching in the prior art, the prior art need only teach other, divergent, solutions to be deemed to teach away from an invention.

Thus, by teaching positively towards certain embodiments or features as being important or preferred, the art provides a motivation for the person skilled in the art to go in a particular direction. If that direction leads towards subject matter outside the scope of the claims at issue, then it constitutes a “teaching away”. Appellants maintain that the person skilled in the art, even if assumed to be contemplating improvements of Rose, would focus on the specific teachings in Rose of embodiments taught to be important, and be motivated to improve those elements. Rose teaches that combining a pharmaceutical candidate with glycoprotein B and thereafter detecting whether the pharmaceutical candidate has bound to the active site of glycoprotein B to be important. Again, per *Baird*, it is well settled that a reference must be considered not just for what it expressly teaches, but also for what it fairly suggests to one who is unaware of the claimed invention. *In re Baird supra*. Rose is clearly directed to the use of combining a pharmaceutical candidate with glycoprotein B, which is described at length from Column 5, line 8 to Column 64, line 55. That is, Rose devotes about 59 columns of text to what is the essence of his invention, the use of combining a pharmaceutical candidate with glycoprotein B. Rose does not teach, suggest, or disclose using NMR spectrum and/or any image observable during the course of the reaction between the candidate and glycoprotein B, as would be required if either of the methods of claims 1 or 10 of the present invention were being used. Instead, the detection step of Rose is temporally separate to the reaction itself.

Since claims 3-9 are dependent on claim 1, this rejection is respectfully traversed on the basis of the argumentation used above for claim 1. Appellants therefore submit that claims 3-9 are inventive over Rose in view of Pines.

Accordingly, as none of the cited references are properly combinable so as to render the present invention obvious, Appellants respectfully request that the Board reverse the Examiner's rejections and direct that claims 1 and 3-10 be allowed.

## **CONCLUSION**

In view of the foregoing, Appellants respectfully request that the Board reverse the rejections of Claims 1 and 3-10 as set forth in the Office Action mailed July 25, 2006, that the Board allow the pending claims since they are in condition for allowance, and that the Board grant any other relief as it deems proper.

Dated: March 26, 2007

Respectfully submitted,

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### **XIII. CLAIMS APPENDIX**

1. An *in vitro* method which is a test involving a reaction of one or more biological molecules and which comprises:  
labeling one of said biological molecules with hyperpolarized  $^{129}\text{Xe}$ , wherein an assay reagent comprises said biological molecules;  
conducting said reaction; and  
observing a magnetic response resonance (NMR) spectrum and/or NMR image of the hyperpolarized  $^{129}\text{Xe}$  during the course of said reaction in order to detect a conformational change in the labeled biological molecule.
2. Cancelled.
3. The method of claim 1, wherein the assay is a competition assay or an immunoassay for following the progress of a reaction selected from the group consisting of receptor-ligand interactions, enzyme-substrate reactions and protein-protein interactions.
4. The method of claim 1, wherein the assay is a hybridization assay or a binding assay for following the progress of a reaction selected from the group consisting of immunoassays for specific analytes, nuclease assays, mutation analysis, mRNA detection and DNA detection.
5. The method of claim 1 wherein the biological molecule is a peptide or a protein.

6. The method of claim 1 wherein the hyperpolarized  $^{129}\text{Xe}$  is enriched at a level of 40% or more.
7. The method of claim 1 wherein the degree of hyperpolarisation is 8% or more.
8. The method of claim 1 which is performed in a solution wherein the solvent has a viscosity in the range of 700 to 1500mPs.
9. The method of claim 1 wherein the pressure of the xenon gas is at least 5 bar.
10. An *in vitro* assay method for following the progress of a reaction of one or more biological molecules and which comprises:
  - labeling an assay reagent with hyperpolarized  $^{129}\text{Xe}$  , wherein said assay reagent comprises one of said one or more biological molecules;
  - conducting said reaction; and
  - observing a change with time of a magnetic response resonance (NMR) spectrum and/or NMR image of the hyperpolarized  $^{129}\text{Xe}$  during the course of said reaction in order to detect a conformational change in the labeled assay reagent.

## **IX. EVIDENCE APPENDIX**

Appellants hereby append copies of the following patents:

U.S. Patent No. 6,015,565 (“Rose”)

U.S. Patent No. 6,426,058 (“Pines”).

This is the evidence relied upon by the Examiner for rejection of appealed Claims 1 and 3-10 in the Office Action dated July 25, 2006.

**X. RELATED PROCEEDINGS APPENDIX**

There are no other appeals or interferences related to the instant appeal.